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STUDIES ON
THE POSTNATAL DEVELOPMENT OF
THE ELECTRORETINOGRAM IN
NEWBORN INFANTS

BY

BIRGITTA ZETTERSTRÖM

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This survey is based on the following six papers :

- A. ZETTERSTRÖM, B., The Electroretinogram in Children During the First Year of Life. (*Acta Ophthal.* 1951, 29, 295.)
- B. ZETTERSTRÖM, B., The Electroretinogram in Prematurely Born Children. (*Acta Ophthal.* 1952, 30, 405.)
- C. ZETTERSTRÖM, B., The Effect of Light on the Appearance and Development of the Electroretinogram in Newborn Kittens. (*Acta Physiol. Scand.* 1956, 35, 272.)
- D. ZETTERSTRÖM, B., Flicker Electroretinography in Newborn Infants. (*Acta Ophthal.* 1955, 33, 157.)
- E. WIRTH, A., and ZETTERSTRÖM, B., Effect of Area and Intensity on the Size and Shape of the Electroretinogram. (*Brit. J. Ophthal.* 1954, 38, 257.)
- F. HELLSTRÖM, B., and ZETTERSTRÖM, B., The Effect of Light on the Manifestation of the Electroretinogram and on Histochemically Demonstrable SH-Groups in the Retina. (*Exptl. Cell Research*, 1956, 10, 248.)



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Introduction

In the present papers, the electroretinogram (ERG) denotes the electric action potential obtained when the retina is exposed to brief illumination after a standardized period of dark adaptation. The electric response to the light stimulus is led off by an active electrode of chlorinated silver inserted in a contact glass filled with physiologic saline, and placed on the anterior surface of the eye. (A special technique was, however, used in E.) The stimulus light is obtained from a 25-watt lamp giving flashes of white light about 0.06 sec. in duration, the required intensity being maintained for about one-third of this time. Since stray light is emitted from the contact glass and the ocular media, the whole retinal area receives a light stimulus; consequently, the potential that arises is a total response of the retina. — The indifferent electrode consists of a silver plate attached to the forehead by a head band.

The potential is recorded by means of a condenser-coupled amplifier with a time constant of 1.5 sec. The potential is photographed together with a record of the light stimulus, from a photocell, and the time marking, the distance between each thin line representing 0.02 sec. In the figures illustrating ERG potentials in the publications to be discussed, the lower curve shows the light marking. For further details, reference is made to Karpe (1948), whose method was applied in all the investigations except E, in which an account is given of the special technique used.

In the first of the present investigations, the ERG was studied in newborn infants. Only the first part of the ERG, comprising the a- and b-wave, was recorded. It was then found that, in newborn infants, it is absent or is exceedingly small. When the development was followed, a slow increase in the ERG was found to take place. In children about one year old, a type of ERG was obtained which was in agreement with that recorded in adults, although the b-potential was slightly below the adult mean (A).

In order to ascertain the cause underlying these findings, investigations were made with a view to elucidating the manifestation and development of the ERG potential. The ERG in premature infants was studied in order to evaluate the influence of the degree of maturity (B). Newborn kittens were examined to determine the development of the ERG when they were reared in light and in darkness, respectively, to permit a study of the possible effect of light on manifestation of the ERG (C). The cat was chosen as the experimental animal in view of the

fact that its retina greatly resembles the peripheral human retina. — The ERG was recorded with variations in the size of the retinal area stimulated (E). The development of the flicker ERG was investigated in newborn and young infants, for the purpose of studying the development of the rod and cone functions (D). In addition, the ERG was correlated with histochemical investigations of the retina in a group of kittens reared in light and in a group reared in darkness (F).

I. Earlier Investigations on Development of the a- and b-Wave of the ERG

Since complete bibliographies of publications dealing with these questions are found in the monographs of Granit (1947, 1955), only those of particular interest in the present connexion are mentioned here. As far as clinical investigations are concerned, changes in the type and size of the ERG have been studied in a number of pathologic conditions. As they have not disclosed any facts that can throw light on postnatal development of the ERG, they are not included.

Although numerous animal experiments have been made with a view to ascertaining the origin in the retina of the components of the ERG, P I, P II and P III, the problem is not yet definitely solved.

The two rapid components, P II and P III, are of interest in the present connexion. Granit (1947) localized P III to both the receptors and neural layers, and P II to the neural layers between the receptors and the ganglion cells.

Ottoson and Svaetichin (1952, 1954), using the micropipette technique on the frog and fish retina, concluded that the ERG potential derives from the receptor layer alone. Tomita and Funaishi (1952) used the microelectrode technique; they found that the bipolar layer could be that in which the ERG potential (a- and b-wave) originates. Tomita and Torihama (1956) later found, with the use of micropipettes less than $1\ \mu$ in diameter, that no potential can be led off in the receptor layer but only directly inside it. The problem of the localization of the ERG is evidently in need of further elucidation.

Noell (1953) produced a selective effect on the structure of different parts of the retina by intravenous administration of various enzyme inhibitors. He therefore concluded that his assumption that "the inner limbs are an essential element for the manifestation of a- and b-waves must take into consideration that physico-chemical changes in the vicinity of the inner limbs seem equally important in producing these electrical reactions and that consequently the inner limb can only constitute one 'electronic' element of the current produced. In case of the a-wave, current flow would probably not develop without specific reaction at the linkage between inner and outer limb, and similarly a b-wave current probably does not ensue unless structures proximal to the inner limbs (*i.e.*, outer plexiform layer) participate in the excitation process". Granit (1955) has also considered this theory to be probable.

Keeler, Sutcliffe and Chaffee (1928) studied development of the ERG in

newborn mice. They demonstrated that the ERG potential appeared after the first 13 days of life, and then fairly rapidly increased to the normal size on about the 25th day. They attributed absence of the ERG to incomplete development of the rod layer and lack of visual purple. Demirchoglian and Mirzoian (1953) showed the same conditions to apply in young rats.

Müller-Limmroth and Andrée (1954) demonstrated in tadpoles that an ERG on stimulation with white light cannot be recorded until the 6th day of life, and that a practically normal response is obtained already on the 17th day. They also stated that higher light intensities are required than in adult animals, in order to produce the maximal response for the age. The ERG with respect to colour stimuli was stated to develop in a similar though slower way. As a probable explanation of the absence of the ERG potential during the first days of life, they suggested a rapid differentiation of some form of precursor substance in the rods and cones, until the final "visual substance" appeared shortly after birth. They also regarded the influence of light to be necessary for this process, mainly with the support of the fact that Birukow and Knoll (1952) succeeded in delaying this differentiation in the retina of tadpoles that had been kept in the dark after birth.

In puppies, the ERG cannot be recorded until the 21st day of life (Parry, Tansley and Thomson 1955), and reaches its full size on the 40th to 50th day. These workers, in similarity to Keeler, Sutcliffe and Chaffee, concluded that incomplete development of the rods and lack of visual purple are responsible for absence of the ERG during the first days of life.

Varying techniques have been applied in the ERG investigations on newborn animals reviewed in the foregoing. Consequently, no direct comparisons can be made between these results and those obtained in the present investigations.

II. Present Investigations

PAPER A

An account is given of ERG investigations in children from birth up to one year of age. As a rule, no potential could be recorded during the first day of life; a suggested ERG was obtained in only 4 out of 35 newborns. Already after one to three days, an incipient ERG appeared in all of them, though it differed in type from that recorded in adults. The b-potential had a somewhat longer latent period and duration, and the negative component, the a-wave, was entirely lacking even with the strongest light stimulus. The first, rising part of the b-wave also had a lower gradient and the duration of the whole b-wave was longer than in adults, *i.e.*, it was flatter.

When recordings were made at rising ages, a measurable ERG was found to have appeared at a few weeks of age. At about three months, a b-potential of approximately 0.10 to 0.20 mV had developed. The latent period of the b-wave had then decreased somewhat, but it was still impossible to record any a-wave, even with a strong light stimulus.

At 5 to 6 months old, the size of the b-potential was 0.20 to 0.30 mV. It was not, however, possible to record an ERG fully in agreement as to type, latency and duration with that of adults until the end of the first year of life. Even then, the size of the b-potential was still 0.20 to 0.30 mV, and thus below the adult mean.

Studied with ordinary histologic technique, the human retina is fully developed at birth except in the macular region, in which a fine differentiation takes place during the first weeks of life (Mann 1928), and is fully developed in every detail after the first few months (Barber 1955). In view of this fact, it is not possible to correlate manifestation of the ERG with morphologic development of the retina, unless studies with the electron microscope were to show immaturity in some of the retinal layers in which the ERG can be supposed to originate. Another possible explanation of development of the ERG is functional immaturity, for example, some form of enzymatic immaturity in the retina.

It is also necessary to take into account the possibility of external stimulating factors, of which light seems to be a likely one. — With a view to obtaining support for this hypothesis, investigations of a similar nature were made in both premature infants, and in kittens that had been reared in darkness.

PAPER B

In this paper, a report is made of ERG investigations in premature infants in the following weight groups: 1,000 to 1,500 g, 1,500 to 2,000 g and 2,000 to 2,500 g. In the lowest weight group, the ERG was not manifested until the 21st to 63rd day of life. In the second group (1,500 to 2,000 g) appearance of the ERG was still delayed as compared to that in full-term infants, but in a few cases it could be recorded as early as the second week. In the highest weight group, an ERG appeared in $\frac{3}{4}$ of the cases during the second week of life, and in the remaining $\frac{1}{4}$ during the third week.

It therefore seems probable that the degree of maturity plays a role in manifestation of the ERG. Presumably, however, it does not alone determine the time for appearance of the ERG in prematures. If this were the case, the ERG of premature infants would appear at calculated term. In the investigation in question, it could be recorded far earlier. This fact seems to substantiate the theory that the light to which the infant is exposed postnatally has a stimulating effect on the retinal functions responsible for appearance of the ERG.

Additional support is given to this theory by studies of manifestation of the ERG in kittens born and reared in darkness, compared to the development in a control group reared in daylight. These investigations are reported in paper C.

PAPER C

In kittens bred in daylight, an ERG could be demonstrated practically at the same time as spontaneous opening of the eyelids, *i.e.*, on the 6th to 10th day of life. When the palpebral fissure was cut apart before spontaneous opening, a b-potential was only exceptionally recorded, and was then extremely small. After about the 10th day, the potential was found to increase rapidly in size, and at 9 to 10 weeks had the same size and appearance as in full-grown cats, *i.e.*, 0.40 to 0.60 mV.

In kittens born and bred in darkness, appearance of the first ERG potential was more delayed in relation to that in kittens bred in daylight. It was not, however, possible to retard manifestation by means of a stay in darkness longer than to about four weeks of age. Before this age, a small b-potential appeared in 13 out of 35 kittens, although they had been reared in darkness. In every case, the mean value of the potential was less than that in kittens of the same age reared in daylight. In the other 22, no b-potential could be recorded. In kittens that had remained in darkness until more than four weeks of age before the first exposure to light took place, a distinct ERG was recorded, of normal size for the age.

In all the animals bred in darkness in which no definite delay in appearance of the ERG was noted beyond that in animals bred in light, there was, however, a distinct prolongation of the latent period of the b-potential during the first weeks of life.

It was found that, once the eye of an animal reared in darkness had been exposed to strong light stimulation — as in an ERG examination — development of the b-potential started. It rapidly attained the same size as that in a kitten of the same age bred in daylight, as a rule on the following day. Thus, no definite difference was noted in development of the ERG if the kittens were kept in darkness after the first exposure to light on ERG recording, or if they subsequently remained in the light.

The influence of light on development of the ERG seems to be of importance, but it is apparently a contributory factor only during a limited period. Kittens kept in darkness for more than four weeks exhibited an ERG normal for their age, despite this fact. After this age, the maturation process in the retina, morphologic or purely functional, evidently proceeds normally despite darkness.

PAPER D

Flicker electroretinography is a method which affords a possibility of distinguishing objectively between the functions of the rod and the cone systems. It is therefore of interest to apply this method in newborn infants, and to compare the results with morphologic development of the macular region and beginning central fixation. An account of investigations with this method is given in paper D.

Analyses of the flicker fusion frequency in infants up to 24 hours old showed it to be usually lacking even at light intensities up to 1,000 lux. In one out of five cases, a low-frequency flicker was recorded that did not exceed a fusion frequency of 15/sec.; it was of scotopic type even at strong intensities of light. The scotopic type denotes a flicker in which the fusion frequency is low, the b-potential has a gently curved shape, and the a-wave is entirely lacking.

At two to three days old, a measurable flicker was present in every case, although it was purely of a scotopic type even at intensities approaching 1,000 lux. It had a maximum fusion frequency of 25/sec. at 200—700 lux. A light intensity of 50—200 lux is required to produce any flicker whatsoever at this age. In adults, a scotopic flicker with a fusion frequency of 10—30/sec. is obtained with a stimulating frequency of about 0.5—5 lux, and at intensities of 10—1,000 lux, a flicker of photopic type is produced, with a fusion frequency of up to 70/sec. (Dodt and Wadensten 1954.) By photopic type is meant a flicker in which the fusion frequency is high, and the individual b-potentials are peaked, and separated by the negative a-waves.

In infants almost one week old, the fusion frequency was found to have risen to about 35/sec. The lowest stimulating intensity eliciting a flicker was 5—10 lux, a maximum fusion frequency being obtained already at 20—500 lux. The flicker ERG no longer exhibited scotopic features only. A transition to a photopic flicker was discernible at high light intensities.

At three weeks of age, a flicker was recorded even at 3—5 lux, and a fusion frequency maximum of 35—40/sec. was reached at 20—500 lux. In 7 out of 11 cases a distinct transition from a scotopic to a photopic type of flicker was observed in recordings at the higher intensities. In the remaining 4 cases, only a scotopic flicker was recorded.

Infants six to eight weeks old exhibited a maximum fusion frequency of about 50/sec. that could not definitely be regarded as differing from that recorded in adults. The lowest intensity at which a flicker was elicited was below 1 lux. A distinct transition from a scotopic to a photopic flicker was found at intensities exceeding about 10 lux.

The flicker recorded in newborn infants and during the first week of life thus has a scotopic appearance, *i.e.*, it is composed of small rounded, b-waves, whereas the a-wave is lacking, even at light intensities of 500 to 1,000 lux. The flicker is also of low frequency, not exceeding 35/sec. Thus, the initial reaction of the retina in a newborn infant is that of a rod-reacting retina, even at high stimulating intensities, contrary to the conditions in the adult retina.

It was found that, using the flicker ERG, the function of the cone system could be recorded objectively in some of the infants examined at three weeks of age, and at six to eight weeks in all of them. In infants, fixation of the eyes becomes stabilized during the sixth to eighth week of life, at the same time that the macula becomes almost fully developed morphologically (Mann 1928). At this time, the photopic flicker electroretinogram characteristic of the cone system was recorded in all the infants in the present investigation.

PAPER E

In many animal species, among them the cat, the postnatal morphologic completion of retinal development takes place from the centre towards the periphery, in the form of a slowly increasing mature area, with a successively larger diameter, finally comprising the whole retinal area (Abelsdorff 1905).

The human retina undergoes similar development prenatally, starting from a circular zone round the macula, and is — as mentioned earlier — fully developed morphologically at birth, except in the macular region (Mann 1928).

It could therefore be supposed that, after birth, the part of the infant retina from which the ERG is elicited would consist of an area increasing from a para-central zone towards the periphery. This could imply that when a sufficient number

of retinal elements are capable of function, a small ERG is first obtained, which subsequently increases in size, as the number of elements that become mature and can participate in the process increases. By a retinal element is meant the functional unit which consists of a ganglion cell in the ganglion cell layer of the retina, and all the synapses coupled to this cell, as well as the sensory cells connected with them (one cone in the macula, or groups of rods and cones in the periphery).

In view of this hypothesis and of the importance of studying the influence of area on the ERG in general, an investigation was made in adult cats of the effect of varying size of the retinal area stimulated and varying intensity of stimulus on the size and shape of the ERG.

The size of the retina stimulated (area) was determined exactly by means of special Perspex cones, 1—1.5—2—3—5 mm in diameter at the top, where the light passed out. Their external surface was blackened in order to avoid stray light. After removal of the cornea and lens, a cone was moved down to the retinal surface by a micromanipulator. Light flashes 1/10 sec. in duration were given at 30-sec. intervals. The stimulus intensity was varied with neutral filters. The ERG was led off by silver silver-chloride electrodes ending in a cotton wick soaked in saline, and applied to the limbus and nose of the animal. The leads were taken to a condenser-coupled amplifier of long time constant and a cathode-ray tube.

In order to obtain an ERG showing the characteristic features of the high-intensity ERG response, it was necessary to use cones with a diameter of 3—5 mm. With smaller area, the response assumed the characteristics of the low-intensity ERG, even at maximum intensity of stimulus. In a few animals, an extremely small, slow ERG was obtained with an area 1 mm in diameter, but the lowest limit usually lay between 1.5 and 2 mm diameter. Below this limit, no ERG could be recorded despite high intensity of the stimulus. In recordings of the flicker ERG, it was found that only high-intensity responses, elicited by large areas, could produce high-fusion frequencies in flicker.

It could therefore be concluded that a definite relation exists between the size of the area and the size of the b-potential. Moreover, there is a relation between the shape of the b-potential and intensity of the stimulus, provided that the area exceeds a certain minimum value.

PAPER F

Sidman and Wislocki (1954) have shown that sulphydryl groups are more abundant in the retina of the adult cat than in that of the newborn kitten. Wald and Brown (1952) have also put forward the hypothesis that the SH-groups play a role in manifestation of the electric reaction of the retina. Against the background of these observations, an account is given in paper F of investigations

with a histochemical staining method (Bennet, cited by Everson Pearse 1953) of the occurrence of SH-groups in the different retinal layers. The experimental animals were kittens born and reared in darkness, and kittens reared in the light. The results were also correlated with manifestation of the ERG potential in these animals.

In the *animals reared in light*, the nuclear layers showed fairly intense SH-staining; after differentiation into outer and inner nuclear layer, the outer stained more strongly, irrespective of age. The ganglion cells stained weakly. The plexiform layers, as well as the rod layer, did not react until about a week after birth, and then only weakly. The membrana limitans externa and interna could not be distinguished.

During the first days of life, the retinae of the *animals reared in darkness* did not differ in these respects from those of the animals reared in light. After a week, a distinct decrease in intensity was observed in the nuclear layers, particularly in the outer; this became increasingly distinct with rising age. Thus, in animals 21 to 23 days old, the outer nuclear layer was extremely weakly stained or not at all. On the other hand, the intrinsically weak staining of the rod layer was unaffected in the animals reared in darkness. In animals bred in darkness but exposed to high light intensities in connexion with ERG recording, the retina presented the same features as that of the animals entirely bred in light.

Using this technique, SH-groups were found to be present in relatively large quantities in the retina of the kittens at birth. When the animals were prevented from exposure to light during their first weeks of life, a considerable decrease seemed to take place in the SH-groups in the nuclear layers. Although these differences seemed to be strongly marked, it is necessary to make the usual reservation applying to all histochemical methods, *i.e.*, that no simple quantitative relation exists between intensity of staining and quantity of reacting substance.

In animals bred in light, no ERG potential could be recorded during about the first 6 to 10 days of life. This can be explained by the immaturity of the retina during this period although, should SH-groups be a prerequisite for manifestation of the potential, they seem to be present fairly abundantly in the retina.

If kittens are born and reared in darkness, it is generally possible to delay appearance of the ERG potential, although for at most about three weeks, despite the fact that morphologic maturation of the retina has continued, irrespective of the stay in darkness.

III. General Discussion and Conclusions

The adult human retina is of mixed type with respect to rods and cones, but with a strong preponderance of rods. Using flicker electroretinography, this retina can be made to react with a predominance of the rod and the cone function, respectively, depending on adaptation conditions and intensity of light stimulus.

The retina of the newborn infant contains less pigment than that of the adult but in other respects, as studied with the morphologic techniques hitherto used, it is mature and fully in agreement with that of the adult, except in the macular region. Despite this, it is generally impossible to obtain any potential in attempts to record the ERG or flicker ERG during the first day of life. After a day or so, a small ERG can, however, be recorded, as well as a scotopic flicker ERG on intermittent light stimulation. Despite high intensities, no signs of cone function can be recorded, *i.e.*, the ERG lacks any signs of negativity. Only a low-frequency flicker of scotopic type is obtained.

Any attempt to evaluate function of the eye of the newborn infant in other respects is difficult. Fixation is known to be lacking during the first weeks of life, a fact that is probably due to immaturity of the macular region, but that may also be cerebrally conditioned. Reaction to light is definitely present, and a distinct even if somewhat slow pupillary reaction, as well as screwing up the eyes against strong light, can be observed in all healthy infants, even in prematures. Peiper's reflex (1926) which implies that, during the first days of life, the child extends its head backwards on entry of strong light, is further proof of reaction to light.

Using Peiper's reflex, Trincker (1955) endeavoured to determine the spectral sensitivity curve of the newborn infant. He showed that, on light adaptation, it seems to be in agreement with that of the adult on light adaptation; on dark adaptation, the maximum of the curve is displaced towards a shorter wave length during the first weeks of life. These results indicate that some cone function is present even at birth.

It is scarcely possible to make any direct comparison between Trincker's results and those obtained in flicker ERG:s in newborn infants. The threshold for the flicker ERG may be considerably higher than the threshold for Peiper's reflex. It is, for example, known that the light threshold value for subjective perception in adults is appreciably lower than that for the ERG (Karpe and Tansley 1948). In studies of development of the ERG in tadpoles, Müller-Limmroth and Andrée (1954) showed that the ERG can be recorded earlier with white stimulating light than with coloured. They interpreted this as probable evidence that rod function starts earlier than cone function in these animals.

*Factors Associated with Development of the ERG
in Newborn Infants*

a. Area

ERG studies with variations in the stimulated area in adult cats have shown that when this area is very small, *i.e.*, less than 2 mm in diameter, only an extremely small ERG is obtained, despite high intensities of stimulus. This ERG agrees as to latent period, duration and size with that recorded in 6 to 10-day-old kittens and in newborn infants on stimulation of the whole retinal surface with strong light.

A possible explanation is that, in the two last-mentioned cases, retinal function is confined to a small central and paracentral area, respectively. It is also conceivable that the first ERG response in the retina of the newborn infant is actually a total response from the whole retinal area, and of a special type owing to the fact that, although all the light-perceptive elements of the whole retinal area are stimulated, they have a high threshold and give a small, sluggish electric action potential, on the grounds of morphologic or functional immaturity. A further possibility is that the maturation process gradually spreads over a large area but only in a few elements per unit of area, and these are initially too sparsely spaced to be led off. The distribution of the electric resistances in the eye at the fully developed state is unknown, nor can it be evaluated in earlier stages, when it may well differ.

It cannot at present be determined which of these modes of function actually applies.

b. Morphologic Immaturity

The maturity of the peripheral part of the retina in the newborn infant makes it unlikely that morphologic reasons are responsible for absence of an ERG at birth. Despite this, there may exist finer details indicating immaturity in the synaptic layer, for example, that cannot be detected with ordinary morphologic technique. This nevertheless seems less probable, in view of the fact that the effect of light has been found to be rapid. For instance, in the kittens reared in darkness in which no ERG was present, an ERG that was as developed as in animals of the same age reared in the light could be demonstrated already on the following day.

Immaturity of the macular region at birth has already been mentioned, but the observation that the cone function could not be recorded in the first week of life lends support to the assumption that the cones in the periphery of the retina also function incompletely at this time. The total number of cones in the adult retina amounts to 4,000,000 to 7,000,000 (Polyak 1941), but the fovea contains only 100,000 to 150,000. It could therefore be expected that, provided their apparatus

were functioning, the peripheral cones would fully suffice for a recordable cone function even on the first few days of life. In the adult, a distinct photopic flicker can be recorded at high light intensities, despite extensive macular damage (Wadensten, unpublished observation). This shows that, even in total absence of macular function, peripheral cone function can be recorded by flicker ERG.

c. Enzymatic-Functional Immaturity

In newborn mice (Keeler, Sutcliffe and Chaffee 1928) and puppies (Parry, Tansley and Thomson 1955) the absence of an ERG during the first days of life has been regarded as due to incomplete development of the rod layer and resulting lack of visual purple, which is formed in the outer segments of the rods (Boll 1876). It seems unlikely that this can be the *only* factor responsible, in view of Noell's investigations (1953). He showed that, on intravenous administration of sodium iodate, most of the outer limb of the rod can be destroyed without producing any definite effect on the size of the a- and b-wave of the ERG. The literature does not seem to contain any statements regarding the presence of visual purple in the retina of newborn infants. There does not, however, seem to be any reason for supposing that it is lacking, in view of the fact that the outer segments of the rods, which are the structures containing the visual purple, are fully developed (Tansley 1933).

There are certainly no grounds for regarding the deficiency of pigment in the retina of the newborn infant as a possible contributory cause to the absence of an ERG. In extreme variants of pigment deficiency, *i.e.*, in adult albinos, a normal ERG can be recorded (Zetterström, unpublished observation). Moreover, it has been shown by Tomita (1950) with microelectrode technique that no ERG can be led off with the electrode in the pigmented layer.

The presence of SH-groups in the retina as a possible prerequisite for recording an ERG in kittens has already been discussed. Wald and Brown (1952) have demonstrated that SH-groups are liberated on bleaching of rhodopsin, and have also ascribed a role to hypothetical SH-groups in eliciting the electric generator potential in the eye. Wald (1953) has also pointed out that the reduction in the retinal potential of experimental animals produced by Noell (1953) with intravenous injection of iodoacetic acid may have been due to a change in the retinal content of SH-groups, since iodoacetic acid is an SH-inhibitor.

d. Light

Several inferences can be drawn from the investigations reported in the foregoing to indicate that light is a stimulating factor for appearance of the ERG in newborns.

The observation that a potential cannot generally be recorded immediately after

birth, but only appears within the next few days, is already an indication that an external stimulating factor can hasten manifestation of the ERG. The fact that an ERG can be recorded in premature infants considerably before calculated term may also support this theory.

Appearance of the ERG in newborn kittens is delayed longer when they are reared in darkness than when they are reared in light. This fact also seems to be an argument in favour of light as a stimulating factor. It was not, as stated earlier, possible to retard the appearance for more than at most three weeks. This fact can be interpreted as an indication that light influences development of the ERG, but that it is active only during a limited period. When the stay in darkness exceeded a certain period, an ERG normal for the age could be demonstrated. Consequently, the morphologic or functional process of retinal maturation had evidently taken place normally, despite darkness. — Additional evidence of light as a stimulator is the following. In those kittens bred in darkness in which an ERG was lacking at the first examination, it was possible already on the following day to record a potential that was as large and as developed as that in animals of the same age reared in the light.

Summary of the Results

1. An ERG is generally absent in newborn infants, but a small potential can always be recorded after the 1st to 3rd day of life. — During the first months of life, the amplitude of the b-potential increases, and is about 0.20 to 0.30 mV at one year, and of the same type as in human adults.

2. In prematures, the ERG cannot be recorded until later than in full-term infants, but nevertheless before calculated term.

3. It is not, as a rule, possible to record a flicker ERG during the first day of life. Thereafter, a low-frequency flicker of scotopic type appears. In the course of the first few weeks, a photopic flicker can also be recorded. At 6 to 8 weeks old, a flicker fusion frequency is obtained that is in agreement with that in adults.

4. Investigations of the size of the stimulated retinal surface (area) necessary for recording of an ERG in the adult cat have shown that the area must not be less than 1.5 mm in diameter. Moreover, a definite relation exists between size of the ERG and size of area.

5. In kittens, a small ERG can be recorded on the 6th to 10th day of life. The potential increases in size during the first weeks, and at 9 to 10 weeks has the same amplitude as in adult cats. — By rearing kittens in darkness, appearance of the ERG can be delayed, but to at most 4 weeks of age. Thereafter, discharges normal for the age are recorded, irrespective of stay in darkness. — In those animals in which manifestation is retarded (before 4 weeks of age), exposure to light results in rapid appearance of an ERG with a size corresponding to that recorded in kittens of the same age reared in the light.

6. Histochemical investigations of SH-groups in the retina of two groups of kittens (one reared in the light and one in darkness) have shown relatively strong staining for SH at birth and during the first days of life. In kittens kept in darkness up to 24 days, the SH-stainability decreases appreciably. These results have been correlated with appearance of the ERG in these animals.

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Errata

- In paper A, p. 295, line 1: *for* eearlier, *read* earlier
p. 299, last line: *for* cones, *read* rods
p. 300, line 8 from foot: *for* enhaled, *read* inhaled
p. 300, line 6 from foot: *for* Ethylalcohol, *read* Ethyl alcohol
p. 301, line 22: *for* darkadaptation, *read* dark adaptation
p. 302, line 16: *for* four months, *read* two months
p. 302, line 13 from foot: *for* with the remets of the ERG records, *read* with the ERG records
p. 303, line 2 from foot: *for* absence, *read* absence
p. 304, line 1: *for* 1949, *read* 1950, and *for* anhydropse, *read* anhydrase
p. 304, line 3: *for* 78:204, *read* 184:109
p. 304, line 7: *for* 1945, *read* 1947
p. 304, line 12: *for* 301, *read* 268
- In paper B, Title: *for* Prematurely Children, *read* Prematurely Born Children
p. 407, line 7: *for* 21—35, *read* 14—35
p. 407, line 8: *for* 21—45, *read* 21—63
- In paper C, p. 273, line 16: *for* occured, *read* occurred
p. 276, line 5: *for* three hours, *read* one hour
p. 277, line 8 from foot: *for* contributory, *read* contributory
p. 278, line 6 from foot: *for* is required in order, *read* is required
p. 279, References, line 6: *for* 148, *read* 141
p. 279, References, line 12: *for* 6.413, *read* 2.413
- In paper D, p. 160, Legend to Fig. 3: *for* left to right, *read* right to left
p. 161, Legend to Fig. 4: *for* left to right, *read* right to left
p. 163, line 1: *for* faculty, *read* frequency
p. 166, line 19: *for* frequence, *read* frequency
p. 166, References, line 4 from foot: *for* 301, *read* 268
- In paper E, p. 259, line 6 from foot: *for* 246, *read* 256
p. 260, line 3 from foot: *for* 1946, *read* 1945

